Claims

1. A Smac protein / carrier entity comprising

   (i) a Smac protein, as disclosed by the GenBank accession number AAF87716, or a derivative or fragment thereof,

   (ii) a carrier

   and wherein the Smac protein, fragment or derivative thereof and the carrier are linked together enabling the penetration of the Smac/carrier entity through the cell membrane into the cell,

   and wherein the carrier is linked to the Smac protein by a chemical bond, and wherein said carrier is selected from the group consisting of TAT, influenza virus hemagglutinin, the VP22 protein from herpes simplex virus, Antennapedia, fibroblast growth factor, Galparan (transportan), poly-arginine, and Pep-1, and fragments and derivatives thereof.

2. The entity according to claim 1, wherein said protein is the TAT protein or a fragment or derivative thereof, as disclosed by GenBank accession number CAA45921.

3. The entity according to claim 1 or 2, wherein the fragment or derivative of the TAT protein comprises the aminoacids 37 to 72 of TAT.

4. The entity according to any of claims 1 to 3, wherein said carrier is the protein transduction domain of TAT comprising the aminoacids 47 to 57 of TAT.

5. The entity according to any of claims 1 to 4, wherein the fragment or derivative of Smac is a peptide comprising the aminoacid sequence 56 to 70.

6. The entity according to any of claims 1 to 5, wherein the fragment or derivative of Smac is a peptide comprising aminoacids 56 to 62 of Smac.

7. The entity according to any of claims 1 to 6, wherein the fragment or derivative of Smac comprises the aminoacids 56 to 59 of Smac.

8. A Smac protein / carrier entity comprising

(i) a Smac protein, as disclosed by the GenBank accession number AAF87716, or a derivative or fragment thereof,

(ii) a carrier,

wherein the Smac protein is a fragment or derivative comprising aminoacids 56 to 62 or 56 to 59 of Smac,

wherein said carrier is the protein transduction domain of TAT comprising the aminoacids 47 to 57 of TAT,

and wherein the Smac protein, fragment or derivative thereof and the carrier are linked together enabling the penetration of the Smac/carrier entity through the cell membrane into the cell,

and wherein the carrier is linked to the Smac protein by a chemical bond.

9. The entity according to any of claims 1 to 8, optionally in combination with at least one active apoptosis-inducing or proliferation-inhibiting compound for use as pharmaceutical.

10. The entity for use as pharmaceutical according to claim 9, wherein the active compound is a cytostatic compound.

11. The entity for use as a pharmaceutical according to claim 9 or 10, wherein the cytostatic compound is selected from the group consisting of antimetabolites, preferably cytarabine, fludarabine, 5-fluoro-2'-deoxyuiridine, gemcitabine, hydroxyurea or methotrexate; DNA-fragmenting agents, preferably bleomycin, DNA-crosslinking agents, preferably chlorambucil, cisplatin, cyclophosphamide or nitrogen mustard; intercalating agents preferably adriamycin (doxorubicin) or mitoxantrone; protein synthesis inhibitors, preferably L-asparaginase, cycloheximide, puromycin or diphteria toxin; topoisomerase I poisons, preferably camptothecin or topotecan; topoisomerase II poisons, preferably etoposide (VP-16) or teniposide; microtubule-directed agents, preferably colcemid, colchicine, paclitaxel, vinblastine or vincristine; kinase inhibitors preferably flavopiridol, staurosporin, STI571 (CPG 57148B) or UCN-01 (7-hydroxystaurosporine); miscellaneous investigational agents, preferably PS-341, phenylbutyrate, ET-18-OCH_3, or farnesyl transferase inhibitors (L-739749, L-744832); polyphenols preferably quercetin, resveratrol, piceatannol, epigallocatechine gallate, theaflavins, flavanols, procyanidins, betulinic acid; hormones preferably glucocorticoids or fenretinide; hormone antagonists, preferably tamoxifen, finasteride or LHRH antagonists; plant-derived cytostatics (from Viscum and derivatives); alcaloids preferably vindesine; podophyllotoxins preferably vinorelbin; alkylants preferably nimustrine, carmustrine, lomustine, estramustrine, melphalam, ifosfamide, trofosfamide, bendamustine, dacarbazine, busulfane, procarbazine, treosulfane, tremozolamide, thiotepa; cytotoxic antibiotics preferably aclarubicine, daunorubicine, epirubicine, idarubicine, mitomycine, dactinomycine; antimetabolites like folic acid analogs preferably methotrexate, purine analogs preferably cladribin, mercaptopurin, tioguanine and pyrimidine analogs preferably cytarabine, fluorouracil, docetaxel; other antineoplastic, platinum compounds preferably thioplatin, carboplatin, oxaliplatin; amsacrine, irinotecane, interferon-α, tretinoine, hydroxycarbamide, miltefosine, pentostatine, aldesleukine; antineoplastic compounds derived from organs, e.g. monoclonal antibodies preferably trastuzumab, rituximab, or derived from enyzmes preferably pegaspargase; endocrine effecting antineoplastic compounds belonging to hormones, e.g. estrogens preferably polyestradiol, fosfestriol, ethinylestradiol, gestagens preferably medroxyprogesterone, gestonoroncaproat, megestrol, norethisterone, lynestrenol, hypothalamus hormones preferably triptoreline,

leuproreline, busereline, gosereline, other hormones preferably testolactone, testosterone; endocrine effecting antineoplastic compounds belonging to hormone antagonists, e.g. antiestrogens preferably toremifen; antiandrogens preferably flutamide, bicalutamide, cyproterane; endocrine effecting antineoplastic compounds belonging to enzyme inhibitors preferably anastrol, exemestane, letrozol, formestane, aminoglutethimide, all of which can be occasionally administered together with so-called protectives preferably calciumfolinat, amifostin, lenograstin, molgromostin, filgrastin, mesna or so-called additives preferably retinolpalmitate, thymus D9, amilomer.

12. The entity for use as a pharmaceutical according to any of claims 9 to 11, wherein the cytostatic compound is selected is from the group consisting of doxorubicin, cisplatin and etoposide (VP-16).

13. The entity for use as a pharmaceutical according to claim 9, wherein the active compound is a death receptor ligand, derivative or fragment thereof.

14. The entity for use as a pharmaceutical according to claim 13, wherein the death receptor ligand is selected from the group consisting of tumor necrosis factor α (TNF-α), tumor necrosis factor β (TNF-β, lymphotoxin-α), LT-β (lymphotoxin-β), TRAIL (Apo2L), CD95 (Fas, APO-1) ligand, TRAMP (DR3, Apo-3) ligand, DR4 ligand, DR6 ligand as well as fragments and derivatives of any of said ligands.

15. The entity for use as a pharmaceutical according to claim 13 or 14, wherein the death receptor ligand is TRAIL.

16. The entity for use as a pharmaceutical according to claim 9, wherein the active compound is an antibody against a death receptor, a derivative or fragment thereof.

17. The entity for use as a pharmaceutical according to claim 16, wherein the antibody against the death receptor ligand is selected from the group consisting of anti-CD95 antibody, anti-TRAIL-R1 (DR4) antibody, anti-TRAIL-R2 (DR5) antibody, anti-DR6 antibody, anti TNF-R1 antibody and anti-TRAMP (DR3) antibody as well as fragments and derivatives of any of said antibodies.

18. The entity for use as a pharmaceutical according to claim 16 or 17, wherein the antibody against the death receptor is the anti-CD95 antibody.

19. The use of Smac/carrier entity according to any of claims 1 to 8, optionally in combination with at least one active apoptosis-inducing compound for the manufacture of a medicament for the treatment of cancer.

20. The use according to claim 19, wherein the cancer to be treated is selected from a group consisting of neuroblastoma, rectum carcinoma, colon carcinoma, familiary adenomatous polyposis carcinoma, hereditary non-polyposis colorectal cancer, esophageal carcinoma, labial carcinoma, larynx carcinoma, hypopharynx carcinoma, tong carcinoma, salivary gland carcinoma, gastric carcinoma, adenocarcinoma, medullary thyroidea carcinoma, papillary thyroidea carcinoma, renal carcinoma, kidney parenchym carcinoma, ovarian carcinoma, cervix carcinoma, uterine corpus carcinoma, endometrium carcinoma, chorion carcinoma, pancreatic carcinoma, prostate carcinoma, testis carcinoma, breast carcinoma, urinary carcinoma, melanoma, brain tumors preferably glioblastoma, astrocytoma, meningioma, medulloblastoma and peripheral neuroectodermal tumors, Hodgkin lymphoma, non-Hodgkin lymphoma, Burkitt lymphoma, acute lymphatic leukemia (ALL), chronic lymphatic leukemia (CLL), acute myeolid leukemia (AML), chronic myeloid leukemia (CML), adult T-cell leukemia lymphoma, hepatocellualar carcinoma, gall bladder carcinoma, bronchial carcinoma, small cell lung carcinoma, non-small cell lung carcinoma, multiple myeloma, basalioma, teratoma, retinoblastoma, choroidea melanoma, seminoma,

rhabdomyosarcoma, craniopharyngeoma, osteosarcoma, chondrosarcoma, myosarcoma, liposarcoma, fibrosarcoma, Ewing sarcoma and plasmocytoma.

21. The use according to claim 19 or 20, wherein the cancer to be treated is selected from the group consisting of neuroblastoma, glioblastoma, breast carcinoma, melanoma, prostate cancer and pancreatic carcinoma.

22. A medicament for the treatment of cancer, comprising a Smac/carrier entity as claimed in any of the claims 1 to 8 and a pharmaceutically acceptable carrier.